ANDA 75-116 October 22, 1999

Keller and Heckman
Attention: John Dubeck
U.S. Agent for: Biovail Laboratories, Inc.
1001 G Street, N.W., Suite 500 West
Washington, DC 20001

Dear Sir:

This is in reference to your abbreviated new drug application dated April 21, 1997, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Diltiazem Hydrochloride Extended-release Capsules USP, (Once-a-Day Dosage), 120 mg,
180 mg, 240 mg, and 300 mg.

Reference is also made to your amendments dated August 18, and October 31, 1997; May 14, June 17, December 22, and December 30, 1998; and August 5, and October 13, 1999.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, your application is tentatively approved. This determination is based upon information available to the Agency at this time, (i.e., information in your application and the status of current good manufacturing practices (CGMPs) of the facilities used in the manufacture and testing of the drug product), and is subject to change on the basis of new information that may come to our attention

The listed drug product referenced in your application, Cardizem® CD of Carderm Capital LP, is subject to periods of patent protection which expire on March 26, 2008, (U.S. Patent 5,002,776); November 14, 2011 (U.S. Patent 5,364,620); August 8, 2012 (U.S. Patent 5,439,689); January 16, 2007 (U.S. Patent 4,894,240); and May 20, 2011 (U.S. Patents 5,470,584 and

5,286,497). Your application contains patent certifications under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use, or sale of Diltiazem Hydrochloride Extended-release Capsules USP (Once-a-Day Dosage), 120 mg, 180 mg, 240 mg, and 300 mg, will not infringe on any of these patents. Section 505(j)(5)(B)(iii) of the Act provides that approval shall be made effective immediately unless an action is brought for infringement of any patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. You have notified FDA that Biovail Laboratories Inc. (Biovail) has complied with the requirements of Section 505(j)(2)(B) of the Act, and that no action for patent infringement was brought against Biovail within the statutory forty-five day period.

However, the Act provides that approval of an abbreviated application such as yours which contains a certification described in Section 505(j)(2)(A)(vii)(IV) (a "Paragraph IV Certification"), and that is for a drug product for which a previous abbreviated application has been accepted that also contains a Paragraph IV Certification, shall be made effective not earlier than one hundred and eighty days after:

a. the date of the first commercial marketing of the drug under the previous application, or

b. the date of a decision of a court holding the patent which is the subject of the certification to be invalid or not infringed, whichever event occurs first (Section 505(j)(5)(B)(iv)).

Furthermore, the district courts in both Inwood and Mova held that 180-days of marketing exclusivity should be granted to the first ANDA applicant who files a Paragraph IV Certification, regardless of whether that applicant is subsequently sued for patent infringement. As a result, the agency will not enforce the "successful defense" provision of Section 314.107(c)(1) and the related provision in 314.107(c)(4). Please be aware that an abbreviated application for Diltiazem Hydrochloride Extended-release Capsules USP, (Once-a-Day Dosage), 120 mg, 180 mg, 240 mg, and 300 mg, containing a Paragraph IV Certification was accepted for filing by this Office prior to the filing of your application. This application was subsequently approved by this office on July 9, 1998 and is

currently being marketed by Andrx Pharmaceuticals, Inc. As noted in the current supplement to the Agency's publication entitled "Approved Drug Products with Therapeutic Equivalence Evaluations", the "Orange Book", the exclusivity granted by the agency to Andrx will expire on December 19, 1999 following 180-days of commercial marketing. Therefore, your application will be eligible for final approval on that date, December 19, 1999.

Because the Agency is granting a tentative approval for this application, please submit an amendment at least 30-days but not more than 60-days prior to the date you believe your application will be eligible for final approval, i.e., December 19, 1999. This amendment should identify changes, if any, in the conditions under which the drug product was tentatively approved, and should include updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate.

Alternatively, this amendment should be submitted stating that no changes have been made to the terms of the application since the date of this tentative approval. This amendment should be designated clearly in your cover letter as a MINOR amendment. In addition to, or instead of this amendment, the Agency may request at any time prior to the date of final approval of this application that you submit an amendment containing the information described above. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

Any changes in the conditions outlined in this abbreviated application as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (CGMPs) are subject to Agency review before final approval of the application will be made.

The drug product that is the subject of this abbreviated application may not be marketed without final Agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug before the effective final approval date is prohibited under Section 501 of the Act. Also, until the Agency issues the final approval letter, this drug product will not be listed in the Agency's "Approved Drug Products with Therapeutic Equivalence Evaluations" list (the "Orange Book").

Prior to submitting an amendment, please contact Timothy Ames, Project Manager, at (301) 827–5798, for further instructions.

Sincerely yours,

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research